

WE CLAIM:

1. A method for treating rosacea in a patient, comprising:

topically administering to a patient in need thereof a storage-stable topical composition in an amount effective to treat said rosacea, wherein said topical composition comprises:

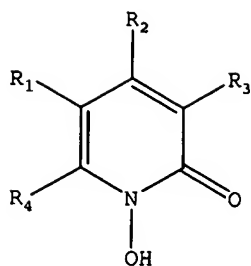
a mixture of an active ingredient comprising an antimicrobial agent or a pharmaceutically acceptable salt thereof, sufficient amounts of at least one pH modifier to provide the topical composition with an overall pH of about 3.0 to about 8.0, and a pharmaceutically acceptable carrier,

wherein said active ingredient maintains a concentration of degradation product(s) that enhances the effectiveness of the topical composition in treating rosacea.

2. The method of claim 1, wherein said active ingredient has a concentration of degradation product(s) less than about 5% of the starting concentration of said active ingredient.

3. The method of claim 2, wherein said active ingredient has a concentration of degradation product(s) less than about 2% of the starting concentration of said active ingredient.

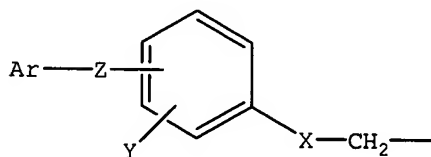
4. The method of claim 1, wherein said antimicrobial agent is a compound having the formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

R_1 , R_2 , and R_3 , which are identical or different, are H or alkyl having 1 to 4 carbon atoms, and R_4 is a saturated hydrocarbon radical having 6 to 9 carbon atoms or a radical of formula II:



II

where:

X is S or O;

Y is selected from the group consisting of H, 1 or 2 identical halogen atoms, and a mixture of 2 different halogen atoms;

Z is selected from the group consisting of a single bond and a bivalent radical comprising O, S, CR_2 where R_2 is H or (C_1-C_4) -alkyl, or from 2 to 10 carbon atoms linked in the form of a chain, which optionally further comprises one or more of the following:

- (i) a carbon-carbon double bond, or
- (ii) O, S, or a mixture thereof, wherein if 2 or more O or S atoms or a mixture thereof are present,

each O or S atom is separated by at least 2 carbon atoms; and,

in any of the foregoing bivalent radicals, free valences of the carbon atoms of said bivalent radical are saturated by H, (C₁-C₄)-alkyl, or a mixture thereof; and

Ar is an aromatic ring system having one or two rings that can be substituted by one, two, or three radicals, which may be identical or different, which are selected from the group consisting of halogen, methoxy, (C₁-C₄)-alkyl, trifluoromethyl, or trifluoromethoxy.

5. The method of claim 4, wherein said antimicrobial agent is selected from the group consisting of 6-[4-(4-chlorophenoxy)-phenoxy-methyl]-1-hydroxy-4-methyl-2-pyridone, 1-hydroxy-4-methyl-6-cyclohexyl-2-pyridone, 1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2-pyridone, a pharmaceutically acceptable salt thereof, and a mixture thereof.

6. The method of claim 5, wherein said antimicrobial agent is 1-hydroxy-4-methyl-6-cyclohexyl-2-pyridone or a pharmaceutically acceptable salt thereof.

7. The method of claim 1, wherein said antimicrobial agent possesses anti-inflammatory properties.

8. The method of claim 1, wherein said topical composition comprises a topical pharmaceutical shampoo comprising:

about 0.5-8% by weight of said active ingredient comprising an antimicrobial agent or a pharmaceutically acceptable salt thereof;

about 0.5-30% by weight of at least one surfactant selected from the group consisting of an amphoteric surfactant, an anionic surfactant, and mixtures thereof;

about 0.01-1% by weight of at least one chelating agent;
and

about 40-90% by weight of purified water;

wherein said at least one pH modifier is selected from the group consisting of pharmaceutically acceptable acids, bases, and mixtures thereof.

9. The method of claim 8, comprising about 1 to about 5% by weight of said active ingredient.

10. The method of claim 8, wherein said at least one surfactant comprises at least one amphoteric surfactant and at least one anionic surfactant.

11. The method of claim 10, wherein said amphoteric surfactant is cocoamidopropyl betaine.

12. The method of claim 10, wherein said anionic surfactant is triethylamine lauryl sulfate.

13. The method of claim 8, comprising about 12-22% by weight of said at least one surfactant.

14. The method of claim 8, wherein said chelating agent is disodium edetate.

15. The method of claim 1, wherein said topical composition has a pH of about 5.5 to about 7.0.

16. The method of claim 15, wherein said topical composition has a pH of about 6.5.

17. The method of claim 8, wherein said pH modifier is selected from the group consisting of sodium hydroxide, citric acid, and a mixture thereof.

18. The method of claim 1, wherein said topical composition further comprises about 0.1-5% by weight of at least one conditioning agent.

19. The method of claim 18, wherein said at least one conditioning agent is selected from the group consisting of a silicone compound, a quaternary ammonium compound, a fatty

compound, a lanolin or a derivative thereof, and mixtures thereof.

20. The method of claim 19, wherein said at least one conditioning agent is a mixture of cetrimonium chloride and ethoxylated polyethylene glycol lanolin.

21. The method of claim 1, wherein said topical composition further comprises an additional ingredient selected from the group consisting of a humectant, inorganic salt, fragrance, dye, hair colorant, foam stabilizer, preservative, water softening agent, and mixtures thereof.

22. The method of claim 1, wherein said topical composition further comprises a thickener selected from the group consisting of methylcellulose, hydroxybutyl methylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, hydroxyethyl ethylcellulose, hydroxyethylcellulose, di(hydrogenated tallow)phthalic acid amide, crosslinked maleic anhydride-methyl vinyl ether copolymer, guar gum, xanthan gum, gum arabic, and mixtures thereof.

23. The method of claim 1, wherein said topical composition is selected from the group consisting of a gel, cream, lotion, suspension, emulsion, ointment, foam, and

mixtures thereof.

24. The method of claim 23, wherein said topical composition is applied with an applicator.

25. The method of claim 24, wherein said applicator is selected from the group consisting of a pledget, a pad, and combinations thereof.

26. The method of claim 1, wherein said topical composition is provided in a package of less than 5 g topical composition as a unit of use.

27. The method of claim 1, wherein said patient is a human female.

28. The method of claim 1, wherein said patient is a human of between 20 and 84 years old.

29. The method of claim 1, wherein said patient is a human of at least 40 years old.

30. The method of claim 1, wherein said rosacea exhibits effects selected from the group consisting of mite organism infestation, erythema, prominent vascularization, dryness, papules, pustules, swelling, telangiectasia, hypertrophy of

the sebaceous glands, nodules, flushing, blushing, rhinophyma, and combinations thereof.

31. The method of claim 30, wherein said mite organism is *Demodex folliculorum*.

32. The method of claim 1, wherein said topical composition is topically applied to sensitive skin areas, irritated skin areas, or inflamed skin areas.

33. A method for reducing or eliminating mite organisms that cause rosacea in a patient, comprising:

topically administering to skin of a patient infected with said mite organisms a storage-stable topical composition in an amount effective to reduce or eliminate said mite organisms, wherein said topical composition comprises:

a mixture of an active ingredient comprising an antimicrobial agent or a pharmaceutically acceptable salt thereof, sufficient amounts of at least one pH modifier to provide the topical composition with an overall pH of about 3.0 to about 8.0, and a pharmaceutically acceptable carrier,

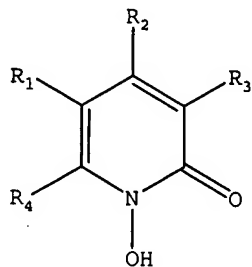
wherein said active ingredient maintains a concentration of degradation product(s) that enhances the effectiveness of the topical composition in reducing or eliminating said mite organisms.

34. The method of claim 33, wherein said mite organisms are *Demodex folliculorum*.

35. The method of claim 33, wherein said active ingredient has a concentration of degradation product(s) less than about 5% of the starting concentration of said active ingredient.

36. The method of claim 35, wherein said active ingredient has a concentration of degradation product(s) less than about 2% of the starting concentration of said active ingredient.

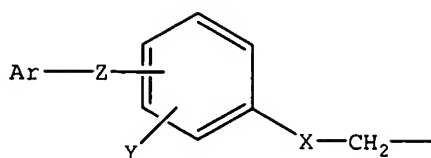
37. The method of claim 33, wherein said antimicrobial agent is a compound having the formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

R_1 , R_2 , and R_3 , which are identical or different, are H or alkyl having 1 to 4 carbon atoms, and R_4 is a saturated hydrocarbon radical having 6 to 9 carbon atoms or a radical of formula II:



II

where:

X is S or O;

Y is selected from the group consisting of H, 1 or 2 identical halogen atoms, and a mixture of 2 different halogen atoms;

Z is selected from the group consisting of a single bond and a bivalent radical comprising O, S, CR₂ where R₂ is H or (C₁-C₄)-alkyl, or from 2 to 10 carbon atoms linked in the form of a chain, which optionally further comprises one or more of the following:

(i) a carbon-carbon double bond, or

(ii) O, S, or a mixture thereof, wherein if 2 or more O or S atoms or a mixture thereof are present, each O or S atom is separated by at least 2 carbon atoms; and,

in any of the foregoing bivalent radicals, free valences of the carbon atoms of said bivalent radical are saturated by H, (C₁-C₄)-alkyl, or a mixture thereof; and

Ar is an aromatic ring system having one or two rings that can be substituted by one, two, or three radicals, which may be identical or different, which are selected from the group consisting of halogen, methoxy, (C₁-C₄)-alkyl, trifluoromethyl, or trifluoromethoxy.

38. The method of claim 37, wherein said antimicrobial agent is selected from the group consisting of 6-[4-(4-chlorophenoxy)-phenoxy-methyl]-1-hydroxy-4-methyl-2-pyridone, 1-hydroxy-4-methyl-6-cyclohexyl-2-pyridone, 1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2-pyridone, a pharmaceutically acceptable salt thereof, and a mixture thereof.

39. The method of claim 38, wherein said antimicrobial agent is 1-hydroxy-4-methyl-6-cyclohexyl-2-pyridone or a pharmaceutically acceptable salt thereof.

40. The method of claim 33, wherein said topical composition comprises a topical pharmaceutical shampoo comprising:

about 0.5-8% by weight of said active ingredient comprising an antimicrobial agent or a pharmaceutically acceptable salt thereof;

about 0.5-30% by weight of at least one surfactant selected from the group consisting of an amphoteric surfactant, an anionic surfactant, and mixtures thereof;

about 0.01-1% by weight of at least one chelating agent;
and

about 40-90% by weight of purified water;

wherein said at least one pH modifier is selected from

the group consisting of pharmaceutically acceptable acids, bases, and mixtures thereof.

41. The method of claim 40, wherein said at least one surfactant comprises at least one amphoteric surfactant and at least one anionic surfactant.

42. The method of claim 33, wherein said topical composition has a pH of about 5.5 to about 7.0.

43. The method of claim 33, wherein said topical composition further comprises about 0.1-5% by weight of at least one conditioning agent.

44. The method of claim 33, wherein said topical composition further comprises an additional ingredient selected from the group consisting of a humectant, inorganic salt, fragrance, dye, hair colorant, foam stabilizer, preservative, water softening agent, thickener, and mixtures thereof.

45. The method of claim 33, wherein said topical composition is selected from the group consisting of a gel, cream, lotion, suspension, emulsion, ointment, foam, and mixtures thereof.

46. The method of claim 45, wherein said topical composition is applied with an applicator.

47. The method of claim 33, wherein said topical composition is provided in a package of less than 5 g topical composition as a unit of use.

48. The method of claim 33, wherein said topical composition is topically applied to sensitive skin areas, irritated skin areas, or inflamed skin areas.

49. A method for treating rosacea in a patient having sensitive skin, comprising:

topically administering to sensitive skin area, irritated skin areas, or inflamed skin areas of a patient in need thereof a storage-stable topical composition in an amount effective to treat said rosacea, wherein said topical composition comprises:

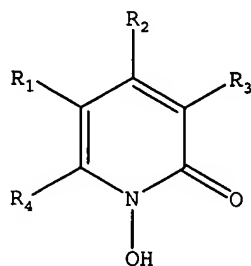
a mixture of an active ingredient comprising an antimicrobial agent or a pharmaceutically acceptable salt thereof, sufficient amounts of at least one pH modifier to provide the topical composition with an overall pH of about 3.0 to about 8.0, and a pharmaceutically acceptable carrier,

wherein said active ingredient maintains a concentration of degradation product(s) that enhances the effectiveness of the topical composition in treating rosacea.

50. The method of claim 49, wherein said active ingredient has a concentration of degradation product(s) less than about 5% of the starting concentration of said active ingredient.

51. The method of claim 49, wherein said active ingredient has a concentration of degradation product(s) less than about 2% of the starting concentration of said active ingredient.

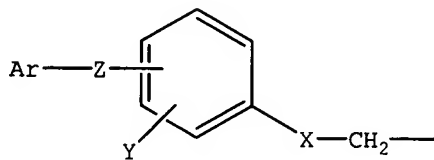
52. The method of claim 49, wherein said antimicrobial agent is a compound having the formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

R_1 , R_2 , and R_3 , which are identical or different, are H or alkyl having 1 to 4 carbon atoms, and R_4 is a saturated hydrocarbon radical having 6 to 9 carbon atoms or a radical of formula II:



II

where:

X is S or O;

Y is selected from the group consisting of H, 1 or 2 identical halogen atoms, and a mixture of 2 different halogen atoms;

Z is selected from the group consisting of a single bond and a bivalent radical comprising O, S, CR₂ where R₂ is H or (C₁-C₄)-alkyl, or from 2 to 10 carbon atoms linked in the form of a chain, which optionally further comprises one or more of the following:

(i) a carbon-carbon double bond, or

(ii) O, S, or a mixture thereof, wherein if 2 or more O or S atoms or a mixture thereof are present, each O or S atom is separated by at least 2 carbon atoms; and,

in any of the foregoing bivalent radicals, free valences of the carbon atoms of said bivalent radical are saturated by H, (C₁-C₄)-alkyl, or a mixture thereof; and

Ar is an aromatic ring system having one or two rings that can be substituted by one, two, or three radicals, which may be identical or different, which are selected from the group consisting of halogen, methoxy, (C₁-C₄)-alkyl, trifluoromethyl, or trifluoromethoxy.

53. The method of claim 52, wherein said antimicrobial agent is selected from the group consisting of 6-[4-(4-

chlorophenoxy)-phenoxymethyl]-1-hydroxy-4-methyl-2-pyridone,
 1-hydroxy-4-methyl-6-cyclohexyl-2-pyridone, 1-hydroxy-4-
 methyl-6-(2,4,4-trimethylpentyl)-2-pyridone, a
 pharmaceutically acceptable salt thereof, and a mixture
 thereof.

54. The method of claim 53, wherein said antimicrobial agent is 1-hydroxy-4-methyl-6-cyclohexyl-2-pyridone or a pharmaceutically acceptable salt thereof.

55. The method of claim 49, wherein said topical composition comprises a topical pharmaceutical shampoo comprising:

about 0.5-8% by weight of said active ingredient comprising an antimicrobial agent or a pharmaceutically acceptable salt thereof;

about 0.5-30% by weight of at least one surfactant selected from the group consisting of an amphoteric surfactant, an anionic surfactant, and mixtures thereof;

about 0.01-1% by weight of at least one chelating agent;
 and

about 40-90% by weight of purified water;

wherein said at least one pH modifier is selected from the group consisting of pharmaceutically acceptable acids, bases, and mixtures thereof.

56. The method of claim 55, wherein said at least one surfactant comprises at least one amphoteric surfactant and at least one anionic surfactant.

57. The method of claim 49, wherein said topical composition has a pH of about 5.5 to about 7.0.

58. The method of claim 49, wherein said topical composition further comprises about 0.1-5% by weight of at least one conditioning agent.

59. The method of claim 49, wherein said topical composition further comprises an additional ingredient selected from the group consisting of a humectant, inorganic salt, fragrance, dye, hair colorant, foam stabilizer, preservative, water softening agent, thickener, and mixtures thereof.

60. The method of claim 49, wherein said topical composition is selected from the group consisting of a gel, cream, lotion, suspension, emulsion, ointment, foam, and mixtures thereof.

61. The method of claim 49, wherein said rosacea exhibits effects selected from the group consisting of mite organism infestation, erythema, prominent vascularization, dryness,

papules, pustules, swelling, telangiectasia, hypertrophy of the sebaceous glands, nodules, flushing, blushing, rhinophyma, and combinations thereof.

62. A method for treating rosacea in a patient, comprising:

topically administering to a patient in need thereof a storage-stable topical composition in an amount effective to treat said rosacea, wherein said topical composition comprises:

a mixture of an active ingredient comprising an antimicrobial agent or a pharmaceutically acceptable salt thereof, sufficient amounts of at least one pH modifier to provide the topical composition with an overall pH of about 3.0 to about 8.0, and a pharmaceutically acceptable carrier,

wherein said active ingredient maintains a concentration of degradation product(s) that enhances the effectiveness of the topical composition in treating rosacea;

and wherein said topical composition is administered concomitantly or sequentially with an additional active agent effective to treat said rosacea.

63. The method of claim 62, wherein said additional active agent is administered with said topical composition either in adjunctive or co-therapy.

64. The method of claim 62, wherein said additional active agent is selected from the group consisting of other macrolide antibiotics, bactericidal drugs, bacteriostatic drugs, cleansing agents, absorbents, anti-infective agents, anti-inflammatory agents, astringents, emollients, moisturizers, keratolytics, retinoids, salts thereof, and mixtures thereof.